*J. Mycopathol. Res.* 64 (3) : i-iii 2026; ISSN : 0971-3719 (Print), 2583-6315 (Online) doi.10.57023/JMycR.64.3.2026.i


# *Editorial*

**From Forest Floor to Nanomedicine: Harnessing Mushrooms for Therapeutic Innovation**

It is well known that mushrooms or macrofungi have served as therapeutic resources in traditional medicinal systems for centuries. Recent advancements in analytical, biochemical, and molecular techniques have furthermore validated their therapeutic potential by unveiling an enormous repertoire of bioactive compounds, viz. phenolics, terpenoids, flavonoids, glucans, and organic acids. These active constituents have exhibited immense pharmacological activities, such as anticancer, antidiabetic, anti-inflammatory, antioxidant, antimicrobial, and immunomodulatory effects. However, the enormous taxonomic and biochemical diversity of macrofungi still remains unmapped, with only a few mushroom species having been systematically studied for their therapeutic potential. This knowledge gap provides a substantial scientific opportunity as well as a promising reservoir for the discovery of new bioactive molecules, therapeutic leads, and mushroom-derived nanotherapeutic strategies. Intensive efforts incorporating mycology, natural-product chemistry, molecular biology, pharmacology, and nanotechnology are therefore necessary to decipher this fundamentally unexploited fungal resource into evidence-based therapeutic applications.

**Discovering Nature's Pharmacy: Pursuit of Mushroom-Derived Therapies against cancer**

The pursuit of precision oncological therapeutics remains a formidable obstacle in modern cancer treatment. While mono-targeted synthetic therapies remain standard in cancer interventions, their adverse side effects have forced the scientific community to revisit nature's repository, championing a multi-targeted, polypharmaceutical approach to combat complex, intricate oncogenic networks.

For more than a decade, our laboratory has pursued a continuous effort to discover the anticancer potential of mushroom species native to the lateritic regions of West Bengal—a chiefly valuable yet underexplored fungal biodiversity. By assimilating traditional ethnomycological knowledge with modern methods in cell and molecular biology, our research has pursued to augment the apparent biological implication of mushrooms beyond their well-known role as nutritional resources and towards their potential as sources of novel therapeutic agents. This work has recognized promising anticancer activities of mushroom-derived extracts and bioactive constituents against miscellaneous malignancies, including leukemia, hepatocellular carcinoma, breast cancer, and lung cancer that together represent the cancer burden in India. These out comes highlight the therapeutic potential of the region's indigenous macrofungal wealth and highlight the significance of systematically investigating its largely untapped chemical and biological diversity.In the last ten years, our team has successfully uncovered the anticancer potential of various macrofungi, including *Amanita princeps*, *Astraeus hygrometricus*, *Macrocybecrassa*, *Lentinus squarrosulus*, and *Termitomyces heimii*, by evaluating various extracts against a wide range of cancer cell lines from different tissue origins. Our investigation uncovers the antileukemic properties of *A. hygrometricus* and *M. crassa* and finds that the ethyl acetate and methanolic extracts of *T. heimii* effectively attenuate hepatocellular and lung carcinoma, respectively.

Moreover, rather than randomly isolating compounds, our study employs bioactivity-guided fractionation to pinpoint lanostane-type triterpenes, astrakurkurone, from *A. hygrometricus* that selectively induce robust apoptosis in MOLT-4 (human acute lymphoblastic leukemia) cells. Further, an in-depth study reveals that the mechanism behind this antileukemic activity is G0/G1-stage phase targeting and triggering a mitochondria-dependent apoptotic pathway, which is backed by the disruption of mitochondrial membrane potential and elevation of reactive oxygen and nitrogen species (ROS and RNS) and driven by modulation of Bcl-2 family proteins and activation of the caspase cascade. Similarly, neoergosterols identified from *T. heimii*by metabolomic profiling were found to significantly attenuate lung cancer progression. Further studies revealed that the neoergosterol-rich methanolic extract induces cell-cycle arrest at the S-phase transition while simultaneously triggering a mitochondria-dependent

apoptotic pathway. Moreover, this active mycocompound reduces cellular migration by modulating a p53-dependent pathway and downregulating the crucial cytoskeletal modulator palladin.

Our research group have adopted a multidisciplinary methodology which includes *in vitro* cellular assays; integrates *in silico* approaches, computational biology, and metabolomic profiling. With this integrated network pharmacology, our team investigates how these novel bioactive molecules interact with complex oncogenic networks and disease pathways. Thus, the journey speed from raw fungal extract to chemical identification of lead molecules is accelerated. However, translating natural extracts into standardized clinical drugs remains a rigorous challenge till date. In spite of this fact, the cell and molecular biology laboratory offers a convincing blueprint for the future by interpreting the molecular secrets of unexploited small bioactive molecules from the forest floor of West Bengal to targeted, natural cancer therapeutics.

**Exploring Mushroomsfor diabetes treatments**

Diabetes mellitus, a chronic metabolic disorder exhibits persistent hyperglycemia due to impaired insulin secretion, insulin action, or both. The ever increasing global burden of diabetes, along with the adverse side effects of the conventional antidiabetic drugs, has roused interest in natural products as complementary therapeutic interventions. As a result, edible mushrooms having medicinal potential have garnered considerable attention because of their diverse bioactive constituents influence multiple glucose homeostasis pathways. Our research study on *Lentinus squarrosulus* provides insights to the antidiabetic potential of mushrooms throughintegrated approach of biochemical, metabolomic, and computational techniques.More than 40 mushroom species, including *Agaricus*, *Pleurotus*, *Grifola*, *Inonotus*, *Antrodia*, and *Trametes*, have been investigated for their potential to improve glucose metabolism in experimental systems as their constituent polysaccharides, phenolic compounds, terpenoids, sterols, and alkaloids act on different diabetic molecular targets.

Inhibition of carbohydrate-digesting enzymes is the major mechanism by which mushrooms help to control diabetes. Pancreatic α-amylase and intestinal α-glucosidase break complex carbohydrates into absorbable glucose. The established therapeutic strategy in type 2 diabetesis to inhibit these enzymes which delay carbohydrate digestion and reduces postprandial hyperglycemia, Oxidative stress is another major contributor to the development and progression of diabetes and its related complications. The generation of reactive oxygen species is promoted by chronic hyperglycemia resulting in cellular injury and impaired insulin signaling. Mushrooms possess huge antioxidant metabolites that counteract this oxidative damage. This antioxidant potential along with its enzyme inhibitory activity reduce oxidative stress associated with diabetic pathology.

Several studies suggest that mushroom-derived compounds may exert multitarget effects by simultaneously reducing carbohydrate digestion, improving insulin signaling, facilitating glucose uptake, and supporting insulin secretion. Such multitarget activity is particularly attractive for diabetes, which involves multiple interconnected metabolic abnormalities.

In conclusion, the reviewed study adds to the growing body of evidence that edible and medicinal mushrooms represent valuable sources of antidiabetic bioactive compounds. *Lentinus squarrosulus* demonstrated antioxidant activity, inhibition of key carbohydrate-digesting enzymes, and contained metabolites with promising drug-like properties. The identification of naltrindole, a unique isoquinoline from *Lentinus squarrosulus* (Mont.,1842) mushroom, has been reported from our group as a promising anti-diabetic drug molecule for the 21st century. It is a multitarget molecule interacting with enzymes and proteins involved in glucose metabolism which illustrates the potential of integrating metabolomics with computational pharmacology in natural product research. While further experimental validation is required, mushrooms may provide novel, multi-mechanistic candidates for the development of safer and more effective interventions against diabetes mellitus.

**Mushroom-Based Strategies Against Visceral Leishmaniasis**

Visceral leishmaniasis (VL) remains one of the gravestignored tropical diseases, excessively affecting populations in resource-limited regions. Despite the accessibility of conventional antileishmanial drugs, including amphotericin B, miltefosine, and paromomycin, disease management continues to be defied by drug-associated toxicity, emerging resistance, limited accessibility, and prolonged or complex treatment regimens. These restrictions emphasize the unrelenting requirement for safer, affordable, sustainable, and environmentally compatible therapeutic strategies. In this context, nature represents an immense and largely untapped reservoir of pharmacologically

active molecules. Among natural resources, mushrooms are particularly promising yet substantially underexplored, harbouring a diverse array of bioactive mycocompounds with reported antimicrobial, immunomodulatory, antioxidant, and antiparasitic properties. Exploring mushroom biodiversity for novel antileishmanial leads could therefore open new avenues for VL management, while simultaneously highlighting the therapeutic value of an underutilized component of fungal biodiversity. Recent scientific studies around the world have provided an idea of mushrooms as a rich source of phytoconstituents having several health-benefiting properties. A systematic review on mushroom-based antileishmanial studies revealed that a wide array of mushrooms from diverse genera like *Astraeus hygrometricus*, *Agaricus blazei, Agrocybe aegerita, Flammulina velutipes, Grifola frondosa, Lentinus strigosus, Merulius incarnatus, Morchella importuna and Russula sp.* have been found to have potent anti-leishmanial, immunomodulatory and apoptosis-inducing properties due to their ability to induce oxidative stress and mitochondrial dysfunction as recurring mechanisms. Apart from these already reported mushrooms, *Amanita princeps*, a wild edible mushroom from the southern part of West Bengal, has been explored as another new alternative for therapeutic innovation against Visceral Leishmaniasis. The hydroalcoholic extract of *A. princeps* is the most effective extract against both promastigotes and amastigotes of the *Leishmania* parasite, with a high selectivity index, supporting its parasite-selective activity. This extract is also able to disrupt the NO–arginase axis, impair antioxidant defence, enhance oxidative stress, induce mitochondrial depolarization, DNA fragmentation, cell-cycle arrest and apoptosis-mediated programmed cell death. Therefore, this mushroom extract is able to interfere with parasite survival pathways and lead them towards death through multifaceted mechanisms. As natural products come with some disadvantages like poor stability, bioavailability and non-specific distribution, nanoparticles can offer a solution to overcome these problems by their synthesis utilizing extract as a biological reducing agent. Thus, ZnO and Ag nanoparticles have been synthesized and properly characterized using complementary physicochemical approaches. An *in vitro* antiparasitic study by MTT assay identified better efficacy and comparatively lower cytotoxicity of ZnO nanoparticles. The effectiveness of ZnO nanoparticles is accompanied by oxidative stress. It enhances ROS and RNS, which impair mitochondrial potential and subsequently damage the cell membrane and nuclear morphology. ZnO nanoparticles also cause cell cycle arrest in the Sub $G_0$-$G_1$ phase, leading towards programmed cell death.

Thus, the journey from a forest-derived mushroom to a standardized, reproducible mushroom extract and ultimately to a biogenic nanotherapeutic demonstrates the incredible translational prospective of fungal biodiversity in natural-product research. Past therapeutic discovery along with this methodology offers a sustainable model for harnessing and preserving natural resources while augmenting the stability, delivery, and biological activity of their valued constituents through nanotechnology. Nevertheless, translating the promise of *Agaricus princeps* from the laboratory to a clinically appropriate therapeutic platform will entaillaboriousexploration of extract standardization, chemical composition, batch-to-batch reproducibility, pharmacokinetics, long-term toxicity, and therapeutic effectiveness in suitable preclinical models. Such systematic substantiation, together with improvements in biotechnology, molecular pharmacology, and nanotechnology, could establish *A. princeps* as a strong preclinical lead and potentially accelerate the discovery and development of safer, effective, and sustainable antileishmanial therapeutics. Ultimately, the convergence of mycology and modern biotechnology may transform the largely untapped fungal wealth of our forests into a valuable resource for next-generation drug discovery.

**Dr. Santanu Paul**
*Professor*
Department of Botany, University of Calcutta
Kolkata 700019, INDIA
Email: spaul_1971@yahoo.com
spbot@caluniv.ac.in